Remarks

In response to the Final Action of December 2, 2004, applicant submitted an amendment under 37 C.F.R. §1.116 and a Notice of Appeal on June 2, 2005. As reported in the Advisory Action of August 26, 2005, the amendment of June 2, 2005 was entered and overcame the 35 U.S.C. §102 rejections, however, the examiner still considered the 35 U.S.C. §103 rejections to be valid. By virtue of the filing of a Request for Continued Examination submitted herewith, applicant requests entry of the present amendment and reconsideration of the §103 rejections in view of the remarks set forth below.

Claims 1-5, 7-15 and 20 are pending in the application. Claims 1-5, 7-15 and 20 have been rejected. Claim 1 has been amended to delete the phrase "inhibitors of cyclooxygenase II". New claim 21 has been added which depends from claim 9. Support for the language in new claim 21 is found in originally filed claim 9 and pages 3-4 of the specification. No new matter has been added.

In the Advisory Action of August 26, 2003 with respect to maintaining the §103 rejection, the examiner stated:

> " Although the amendment has overcome the 102 rejection, the examiner still considers the 103 rejection to be valid. Dimitroff et al. disclose that PD173074, which can be considered an inhibitor of VEGF (page 121), exhibits anti-angiogenesis effects on corneal neovascularization (Page 122, 2nd paragraph). Therefore, it would be obvious to use PD173074 as an anti-angiogenic agent."

The arguments below are proffered in response to the examiner's statement in the Advisory Action and the §103 rejections remaining in the final action of December 2, 2004.

Claims 1, 3, 18 and 19 have been rejected under 35 U.S.C. §103(a) as being unpatentable over U.S. Patent 6,297,228 (Clark) in view of Dimitroff et al.

Clark describes a method of treating neovasculature in a subject by administering an effective amount of an angiostatic steroid, anecortave acetate, to the subject, administering an effective amount of a photosensitive agent to the subject and irradiating the neovasculature with light having a wavelength absorbable by the photosensitive agent. As acknowledged by the examiner, Clark does not disclose wherein the anti-angiogenic agent is selected from the group consisting of inhibitors of protein kinase C, antagonists of growth hormone, antagonists of vascular endothelial growth factor, antagonists of angiotensin II, antagonists of NF kappa B and phospholipase A2 antagonists.

Dimitroff et al. is directed to studies that investigated the effects of combination treatments involving photodynamic therapy (PDT) and the specific tyrosine kinase inhibitors, PD166285 and PD173074, on suppressing or delaying tumor regrowth. Indeed, all of the combination treatments were carried out to assess their effect on tumor regrowth. None of the

studies in Dimitroff et al. teach or specifically suggest that a combination treatment of PDT and PD166285, PD173074 or other antiangiogenic agents recited in claim 1 would also be effective in treating unwanted ocular neovascularization in a subject suffering from choroidal or retinal neovascularization.

With respect to the examiner's statement that "Dimitroff et al. disclose that PD173074, which can be considered an inhibitor of VEGF (page 121), exhibits anti-angiogenesis effects on corneal neovascularization (page 122, 2nd paragraph)", the examiner appears to be of the opinion that because an anti-angiogenic inhibitor is effective in inhibiting corneal neovascularization, there would be a reasonable expectation that the anti-angiogenic inhibitor would also be effective in combination with PDT to treat unwanted ocular neovasculature in patients suffering from choroidal or retinal neovascularization. However, corneal neovascularization being a condition in the front of the eye is a completely different eye condition from choroidal and retinal neovascularization which is a condition in the back of the eye. That these conditions are completely different and that an anti-angiogenic agent can be effective in inhibiting and treating corneal neovascularization but not effective when given in combination with PDT to treat choroidal or retinal neovascularization is illustrated in Ciulla et al., Exp. Opin. Invest. Drugs, Vol. 8 (12), pp. 2173-2182, 1999 [Ciulla et al., cited in the IDS]. Ciulla at page 2177, first column, first paragraph, indicate that the anti-angiogenic agent, thalidomide, effectively inhibited angiogenesis in a rabbit corneal micropocket assay using basic fibroblast growth factor as well as VEGF. Ciulla et al. further indicate that thalidomide failed to prevent recurrent neovascularization in a patient who underwent PDT for choroidal neovascular membrane formation. Thus, Ciulla et al. make clear that one skilled in the art would not be able to expect effectiveness of an anti-angiogenic agent used in combination with PDT to treat unwanted neovasculature in a subject suffering from choroidal or retinal neovascularization based on the anti-angiogenic agent's effectiveness in inhibiting corneal neovascularization.

Further, applicant respectfully directs the examiner's attention to the Federal Court's instruction in *In re Gurley*, 31 USPQ2d 1131 (Fed. Cir. 1994), wherein the Court instructed that a prior art reference "teaches away" when one of ordinary skill, upon reading the reference, would be discouraged from following the path set out in the prior art reference, or alternatively, would be led in a direction divergent from the path that was taken by the applicant.

In view of the above instruction, it can fairly be said that Ciulla et al., in evaluating the effectiveness of thalidomide in combination with PDT to treat choroidal neovascular membrane formulation, and in their finding that thalidomide failed to prevent recurrent neovascularization in a patient who underwent PDT for choroidal neovascular membrane formation, specifically teach away from the presently claimed method for treating unwanted ocular neovasculature in a subject suffering from choroidal or retinal neovascularization utilizing PDT and the anti-angiogenic agents as set forth in amended independent claim 1.

Accordingly, in view of 1) the lack of suggestion in Dimitroff et al. to utilize the recited anti-angiogenic agents of claim 1 in combination with PDT to treat unwanted neovasculature in a subject suffering from choroidal or retinal neovascularization; 2) the finding in Ciulla et al. that one skilled in the art cannot expect that a combination of PDT and an anti-angiogenic agent would be effective in treating choroidal or retinal neovascularization based on the effectiveness of the anti-angiogenic agent in inhibiting corneal neovascularization; and 3) the teaching away in Ciulla et al. from utilizing a combination of an anti-angiogenic agent and PDT to treat unwanted neovasculature in a patient suffering from choroidal or retinal neovascularization, one skilled in the art reading Clark, Dimitroff et al. and Ciulla et al. would not have been motivated to arrive at a method for treating unwanted neovasculature in a subject suffering from choroidal or retinal neovascularization utilizing a combination of an anti-angiogenic agent and PDT as set forth in amended independent claim 1.

In view of the above, withdrawal of the rejection of claims 1, 3, 18 and 19 under 35 U.S.C. §103(a) is respectfully requested.

Claims 2, 4, 5 and 13-15 have been rejected under 35 U.S.C. §103(a) as being unpatentable over Clark in view of Dimitroff et al..

The arguments proffered above in addressing the rejection of claims 1, 3, 18 and 19 under 35 U.S.C. §103(a) apply equally well to the rejection of claims 2, 4, 5 and 13-15 which depend from claim 1, namely, that since 1) Clark fails to teach or specifically suggest an anti-angiogenic agent selected from the group consisting of inhibitors of protein kinase C, antagonists of growth hormone, antagonists of vascular endothelial growth factor, antagonists of angiotensin II, antagonists of NF kappa B and phospholipase A2 antagonists; 2) Dimitroff et al. fail to teach or specifically suggest utilizing the recited anti-angiogenic agents of claim 1 in combination with PDT to treat unwanted neovasculature in a subject suffering from choroidal or retinal neovascularization; 3) Ciulla et al. teach that one skilled in the art cannot expect that an anti-angiogenic agent effective in inhibiting corneal neovascularization would also be an effective agent in combination with PDT to treat choroidal or retinal neovascularization; and 4) Ciulla et al. teach away from utilizing a combination of an anti-angiogenic agent and PDT to treat choroidal or retinal neovascularization, one skilled in the art reading Clark, Dimitroff et al. and Ciulla et al. would not have been motivated to arrive at a method for treating unwanted neovasculature in a subject suffering from choroidal or retinal neovascularization utilizing a combination of an anti-angiogenic agent and PDT as set forth in amended independent claim 1. Accordingly, the combination of Clark and Dimitroff et al. does not make obvious the presently claimed method as defined in claims 2, 4, 5 and 13-15.

In view of the above, withdrawal of the rejection of claims 2, 4, 5 and 13-15 under 35 U.S.C. §103(a) is respectfully requested.

Claims 11 and 12 have been rejected under 35 U.S.C. §103(a) as being unpatentable over Clark in view of Dimitroff et al. and further in view of U.S. Patent 5,770,619 (Richter et al.).

The arguments proffered above in addressing the rejection of claims 1, 3, 18 and 19 under 35 U.S.C. §103(a) apply equally well to the rejection claims 11 and 12 which depend from claim 1, namely since 1) Clark fails to teach or specifically suggest an anti-angiogenic agent selected from the group consisting of inhibitors of protein kinase C, antagonists of growth hormone, antagonists of vascular endothelial growth factor, antagonists of angiotensin II, antagonists of NF kappa B and phospholipase A2 antagonists; 2) Dimitroff et al. fail to teach or specifically suggest utilizing the anti-angiogenic agents recited in claim 1 in combination with PDT to treat unwanted neovasculature in a subject suffering from choroidal or retinal neovascularization; 3) Ciulla et al. teach that one skilled in the art cannot expect that an anti-angiogenic agent effective in inhibiting corneal neovascularization would also be an effective agent in combination with PDT to treat choroidal or retinal neovascularization; 4) Ciulla et al. teach away from utilizing a combination of an anti-angiogenic agent and PDT to treat choroidal or retinal neovascularization; and 5) Richter et al. do not teach or specifically suggest a combination of PDT and the anti-angiogenic agents recited in claim 1 to treat choroidal or retinal neovascularization, one skilled in the art reading Clark, Dimitroff et al., Richter et al. and Ciulla et al. would not have been motivated to arrive at a method for treating unwanted neovasculature in a subject suffering from choroidal or retinal neovascularization utilizing a combination of an anti-angiogenic agent and PDT as set forth in amended independent claim 1. Accordingly, the combination of Clark, Dimitroff et al. and Richter et al. does not make obvious claims 11 and 12.

In view of the above, withdrawal of the rejection of claims 11 and 12 under 35 U.S.C. §103(a) is respectfully requested.

Claims 11 and 12 have been rejected under 35 U.S.C. §103(a) as being unpatentable over Dimitroff et al. in view of Richter.

The arguments proffered above in addressing the rejection of claims 1, 3, 18 and 19 under 35 U.S.C. §103(a) apply equally well to this rejection of claims 11 and 12, namely that 1) Dimitroff et al. fail to teach or specifically suggest utilizing the anti-angiogenic agent recited in claim 1 in combination with PDT to treat unwanted neovasculature in a subject suffering from choroidal or retinal neovascularization; 2) Ciulla et al. teach that one skilled in the art cannot expect that an anti-angiogenic agent effective in inhibiting corneal neovascularization would also be an effective agent in combination with PDT to treat choroidal or retinal neovascularization; 3) Ciulla et al. teach away from utilizing a combination of an anti-angiogenic agent and PDT to treat choroidal or retinal neovascularization; and 4) Richter et al. do not teach or specifically suggest a combination of PDT and the anti-angiogenic agents recited in claim 1 to treat choroidal or retinal neovascularization, one skilled in the art reading Dimitroff et al., Richter et al., and Ciulla et al. would not have been motivated to arrive at a method for treating unwanted neovasculature

in a subject suffering from choroidal or retinal neovascularization utilizing a combination of an anti-angiogenic agent and PDT as set forth in amended independent claim 1. Accordingly, the combination of Clark and Dimitroff et al. does not make obvious claims 11 and 12.

In view of the above, withdrawal of the rejection of claims 11 and 12 under 35 U.S.C. §103(a) is respectfully requested.

A good faith effort has been made to place the present application in condition for allowance. If the examiner believes a telephone conference would be of value, he is requested to call the undersigned at the number listed below.

Respectfully submitted,

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